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10/622,377	07/18/2003	Thomas J. Jentsch	59572(46865)	9926

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EXAMINER

HAMA, JOANNE

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/622,377	Applicant(s) JENTSCH, THOMAS J.	
	Examiner Joanne Hama, Ph.D.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-67 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant filed a response to the Non-Final Action of May 19, 2005 on December 27, 2005. Claims 1-41 are cancelled. Claims 42-67 are new.

Claims 42-67 are under consideration.

Priority

A certified copy of 10102977.2 application filed in Germany on January 23, 2001 has not yet been received. Applicant indicates a request has been made to the German office and will submit the application upon receipt (Applicant's response, page 7).

Information Disclosure Statement

Applicant indicates that one reference cited on pages 15-24 of the specification has not been listed in a previously filed Information Disclosure Statement. Applicant indicates that an IDS listing that reference will be provided. It is noted that the IDS has not yet been provided.

Withdrawn Rejections

35 U.S.C. § 101

Applicant's arguments, see pages 8-13, filed December 27, 2005, with respect to the rejection of claims 26, 29, 30, 38-40 have been fully considered and are persuasive. The rejection of claims 26, 29, 30, 38-40 has been withdrawn.

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35 U.S.C. § 112, 2nd parag. "use claims"

Applicant's arguments, see page 8 of Applicant's response, filed December 27, 2005, with respect to claims 32-37 as being indefinite because of a lack of recitation of specific method steps involved in the claimed 'use' have been fully considered and are persuasive. Applicant has cancelled claims 32-37 and has amended the claim language in claims 59-64. The rejection of claims 32-37 has been withdrawn.

35 U.S.C. 102(a)

Applicant's arguments, see page 22-23 of Applicant's response, filed December 27, 2005, with respect to the rejection of claim 26 have been fully considered and are persuasive. Applicant has canceled the claim. The rejection of claim 26 has been withdrawn.

35 U.S.C. 103(a)

Applicant's arguments, see pages 23-30 of Applicant's response, filed December 27, 2005, with respect to the rejection of claim 26 and 38 under 103(a) have been fully considered and are persuasive. Applicant has canceled the claims. The rejections of claims 26 and 38 has been withdrawn.

New/Maintained Rejections

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 42-67 are newly rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 42-58 are drawn to cells. This includes naturally occurring cells that have not seen the "hand of man." Using the words, "recombinant," "in vitro," or "isolated" to describe the cells would overcome the rejection. Claims 59-67 depend on claims 42-58 and are thus included in the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-67 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1) an isolated mouse or human muscle cell or a cell line comprising a disruption in its endogenous CIC-1, and a cell membrane preparation or cell vesicle obtained from said cell or cell line,

an isolated mouse or human cell or a cell line obtained from the thick ascending limb of Henle loop, the distal convoluted tubule, the acid-transporting intercalated cells of the collecting duct, and epithelial cells of the inner ear, wherein said cell or cell line comprises a disruption in its endogenous CIC-Kb, and a cell membrane preparation or cell vesicle obtained from said cell or cell line,

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an isolated mouse or human cell or cell line obtained from the proximal tubule of the kidney comprising a disruption in its endogenous CIC-5, and a cell membrane preparation or cell vesicle obtained from said cell or cell line, and

an isolated mouse or human osteoclast or osteoclast cell line comprising a disruption in its endogenous CIC-7, and a cell membrane preparation or cell vesicle obtained from said osteoclast or osteoclast line

does not reasonably provide enablement for

1) any cell, cell line, or cell membrane preparation, or cell vesicle comprising:

a) any disruption in CIC-2,

b) any disruption in CIC-3,

c) any disruption in CIC-Ka,

d) any disruption in CIC-4,

e) any disruption in CIC-6,

f) any multiple disruptions in CIC-1, CIC-2, CIC-Ka, CIC-Kb, CIC-3, CIC-4, CIC-5, CIC-6, or CIC-7,

g) any overexpression of CIC-1, CIC-2, CIC-Ka, CIC-Kb, CIC-3, CIC-4, CIC-5, CIC-6, or CIC-7,

2) any method of using any cell, cell line, or cell membrane preparation, or cell vesicle comprising:

a) any disruption in CIC-2,

b) any disruption in CIC-3,

c) any disruption in CIC-Ka,

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d) any disruption in CIC-4,

e) any disruption in CIC-6,

f) any multiple disruptions in CIC-1, CIC-2, CIC-Ka, CIC-Kb, CIC-3, CIC-4, CIC-5, CIC-6, or CIC-7

g) any overexpression of CIC-1, CIC-2, CIC-Ka, CIC-Kb, CIC-3, CIC-4, CIC-5, CIC-6, or CIC-7.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At the time of filing, the art teaches that a mutation in the CIC-1 gene results in myotonia in humans (Groneimeier et al., 1994, JBC, 269: 5963-5967, also Nilius and Droogmmans, 2003, Acta Physiol. Scand., 177: 119-147, Table 2), the disruption of CIC-Kb results in hypokalaemia, elevated serum bicarbonate levels, salt-wasting, and dehydration resulting from a failure of normal transit of chloride across the basolateral membrane into the bloodstream and deafness (Simon et al, 1997, Nature Genetics, 17: 171-178, previously cited), the disruption of CIC-5 results in Dent's disease characterized by kidney stones, nephrocalcinosis, rickets, and renal failure (Gunter et al., 1998, PNAS, USA, 95: 8075-8080, previously cited), and disruption of CIC-7 in mouse results in osteopetrosis (Kornak et al., 2001, Cell, 104: 205-215). In the case of CIC-Ka, no known human mutations have been reported (Jentsch et al., 2005, 115: 2039-2046, page 2042, 1st col., 3rd parag.); in the case of CIC-2, CIC-3, CIC-4, CIC-6, no known human disease or disorder has been associated with these channels (Nilius

and Droogmans, Table 2). While the art teaches that homologous recombination, as a method of generating targeted disruptions in a gene of interest in a genome, is well known, the art teaches that phenotypes exhibited by the mice associated with the gene disruption are not predictable. At the time of filing, the art did not consider the phenotype of a knock-out or transgenic mouse to be predictable. In addition, the art did not consider the correlation between any observed mouse phenotypes and human disease phenotypes as predictable. Doetschmann et al. teaches that “[o]ne often hears the comment that genetically engineered mice, especially knockout mice, are not useful because they frequently do not yield the expected phenotype, or they don’t seem to have any phenotype” (Doetschmann, 1999, Lab. Animal Sci., 49: 137-143, see page 137, 1st col., 1st parag.). Doetschmann provides numerous examples of instances in which genes considered well-characterized *in vitro* have produced unexpected phenotypes or indiscernible or no phenotypes in transgenic or knockout mice. Moens et al. further teaches that different mutations in the same gene can lead to unexpected differences in the phenotype observed. Moens et al. shows that two mutations produced by homologous recombination in two different locations of the N-myc gene produce two different phenotypes in mouse embryonic stem cells, one leaky and one null (Moens et al., 1993, Development, 119: 485-499). Further, the art demonstrates the unpredictability of making a mouse model for human disease by disrupting the murine gene. Jacks et al. teaches that although retinoblastoma (Rb) gene mutations in humans are associated with retinal tumors, Rb gene knockout mice had tumors in the pituitary gland rather than the retinas (Jacks et al., 1992, Nature, 359: 295-300). Likewise,

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whereas HPRT deficiency in humans is associated with Lesch-Nyhan syndrome, a severe neurological disorder, HPRT-deficient mice are phenotypically normal (Kuehn et al., 1987, *Nature*, 326: 295-298 and Jaenisch, 1988, *Science*, 240: 1468-1474). Thus, the art at the time of filing clearly establishes the unpredictability of determining the phenotype of transgenic or knockout mouse even when the activity of the gene has been extensively studied *in vitro*, and further establishes the unpredictability of generating a mouse model for human disease based on the activity of the gene in humans.

In addition to the phenotypes of knockout mice being unpredictable, the art teaches that while the promise of gene targeting had been to reveal the *in vivo* function of a gene of interest, the functional relevance of gene targeting has been questioned because the mutation might lead to an avalanche of compensatory processes (up- or downregulation of gene products) and resulting secondary phenotypical changes. Thus, a null mutant organism might not only lack the produce of a single gene, but might also possess a number of developmental, physiological, or even behavioral process that have been altered to compensate for the effect of the null mutation (Gerlai, 1996, *Trends Neurosci*, 19: 177-181, page 177, 1st col., 1st parag.). Gerlai teaches an example wherein background genotype can confound the exhibited phenotypes. Targeted disruption of a gene of interest, α , might lead to changes in expression of alleles b and B for gene β . A regulatory change in gene β might lead to different phenotypic changes, depending on which allele (b or B) is present in the organism with the null mutation in gene α . The upshot of this problem is that due to this polymorphism

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in the genetic background, one cannot conclude for certain that a phenotypic change exhibited in a null-mutant mouse resulted from the null mutation or to the genetic background (Gerlai, page 177, 1st col., under "Polymorphism in the genetic background might make the results of gene-targeting studies difficult to interpret").

In addition to these issues, Racay, 2002, Bratisl Lek Listy, 103: 121-126, teaches that:

"mutations of some genes led to phenotype showing severe defects, which did not correspond to any clinically important disorder, indicating either high *in vivo* stability of the gene or the interspecies differences. From the view of human medicine, the differences among the species (it means the differences in genetic background, gene expression, metabolism, and signal transduction) represent the main limitation of the use of genetically modified animals as models of human diseases. Therefore some results acquired by this approach can not be applied in human medicine because of the differences between rodents and human beings (Racay, page 124, under point 5)."

As such, while the knockout mouse may exhibit a phenotype, the phenotypes of the knockout mouse are not necessarily readily applicable to the human condition.

Subsequently, the mouse has no apparent use or application. This issue is seen in the chloride channel field. Mice comprising a disruption in CIC-2 exhibit degeneration in the testis and retina, no known human disease directly connected with CIC-2 have been reported (Nilius and Droogmans, page 123, 2nd col., 1st parag. and Table 2). A disruption in CIC-K1 in mice results in nephrogenic diabetes insipidus, while a disease in humans for the homologous gene, CIC-Ka, is not known (Jentsch et al., page 2042, 1st col., 3rd parag. and Nilus and Droogmans, Table 2). Similarly, while the mouse comprising a disruption in CIC-3 exhibits degeneration of the hippocampus and retina,

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no known human condition has been associated with CIC-3 (Nilus and Droogmans, Table 2). Because there is no known human condition similar to what is seen in the knockout mouse models, an artisan does not know how to use any of the cells obtained from the transgenic mouse comprising a disruption in CIC-2, CIC-K1, or CIC-3.

It is understood that the claims are drawn to cells and not to knockout animals. However, the ability to use the claimed cells stems from whether an artisan could use the cells in the context that a relationship is known between the gene of interest and the human disease or condition. That is, it is not enough to say that minimally, the claimed cells could be used in general studies to determine the pH or electrophysiological status of a cell. Further, the general function of a chloride channel, which allows chloride ions to pass through a cellular membrane, does not provide guidance for an artisan to use specific channels (e.g. CIC-1 versus CIC-5) in the context for which there is a relationship with a human disease. The enabled use of the claimed cell hinges upon the fact that the cell in an *in vitro* assay stems from the understanding what biological characteristics the specific chloride channel has with pathology of a human disease. Subsequently, because CIC-4 and CIC-6 have no known pathology associated with them (e.g. see Nilus and Droogmans, Table 2), the use of cells comprising disruptions in these channels is not enabled.

That said, because the use of the cells depends on the disease, an artisan would know how to use cells obtained from tissues or organs associated with the human disease. In the case of CIC-1, skeletal muscle is affected (Nilus and Droogmans, page 140, 1st col., 2nd parag.). In the case of CIC-Kb, the thick ascending limb of Henle loop,

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the distal convoluted tubule, the acid-transporting intercalated cells of the collecting duct in the kidney, and epithelial cells of the inner ear are affected (Jentsch, page 2041, 1st col., 2nd parag. under "ClC-K/barttin: basolateral chloride channels in kidney and inner ear epithelia"). In the case of ClC-5, ClC-5 and cells in the proximal tubule of the kidney have been demonstrated to have a relationship during the disease (Jentsch, page 2042, 2nd col., 2nd parag. under "ClC-5, endocytosis, and Dent disease"). In the case of ClC-7, there is a relationship between ClC-7 and osteoclasts (Jentsch, page 2044, 2nd col., parag. under "ClC-7: role in osteopetrosis"). As this applies to the instant invention, the use of the cells comprising a specific disruption in a chloride channel depends upon which cells are implicated in the human disease or disorder. It is noted that in light of the teachings of Racay, above, the scope of the cells is limited to human and mouse cells, as an artisan cannot predictably arrive at cells obtained from other animals.

With regard to the issue that the claimed invention is not enabled for cells comprising transgene constructs overexpressing any chloride channel(s) of interest, as neither the art or specification provide any guidance for an artisan to arrive at the claimed invention. While it is understood that the methods of transgenesis and transfection are well known in the art, the issue at hand is whether or not an artisan is enabled to use the claimed invention. At the time of filing nothing in the art or the specification teaches any human condition associated with the overexpression of any chloride channel. Further, at the time of filing, the art teaches that overexpression of a gene of interest does not necessarily result in an animal with a predictable phenotype. For example, Duff et al., 1996, Nature, 383: 710-713 teach that while transgenic mice

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expressing mutant presenilin1 (M146V) exhibit an increase in brain A β 42 plaque formation, transgenic mice that express wild type presenilin 1 (PS1) do not exhibit any increase in brain A β 42 plaque formation (Duff et al. page 711, 1st col., 3rd parag., lines 3-6). Duff et al.'s results teach that an artisan cannot predict that overexpression of any transgene would necessarily result in a phenotype. Alternatively, the art teaches that transgenic mice expressing full length human apo B100 mRNA does not significantly edit human apo B mRNA despite normal editing of endogenous mouse apo B mRNA. Davidson concludes that there may be some species specificity to apo B RNA editing (Davidson, U.S. Patent, 5,434,058, patented July 18, 1995, col. 17, 5th parag.). Thus, the art teaches that one cannot predict that a heterologous mRNA can be processed in a transgenic animal. As these issues apply to the instant invention, an artisan cannot predict that overexpression of a gene of interest results in a transgenic animal exhibiting any phenotype and whether that transgenic animal is a model for a human disease or condition. As such, an artisan cannot obtain a cell from any transgenic animal overexpressing a chloride channel of interest. Further, an artisan is not enabled for the use of any chloride channel in any cell. Similar to the issues concerning cells comprising a disruption in a chloride channel of interest, it is not enough to say that minimally, the claimed cells could be used in general studies to determine the pH or electrophysiological status of a cell. Again, a general function of a chloride channel does not necessarily enable an artisan to practice the claimed invention as it pertains to specific chloride channels. As such, an artisan is not enabled to use any cell overexpressing any chloride channel.

Regarding the issue that the claimed cells comprise multiple overexpression constructs and/or disruptions of chloride channels of interest, the art teaches unpredictability in arriving at the claimed invention. First, regarding the issue of multiple overexpression constructs in cells, the art teaches that an artisan cannot predict what overall phenotype occurs following the expression of multiple transgenes. Siegel et al., 2000, Bioessays, 22: 554-563 teach that mice comprising two transgenes do not necessarily exhibit phenotypes that are the simple combination or an additive result of the two transgenes. Siegel et al. teach that in some cases, mice comprising two transgenes exhibit a phenotype resulting from a synergistic interaction between the two transgenes (Siegel et al., page 559, 2nd col., 1st parag.). Alternatively, Siegel et al. teach that some transgene combinations result in mice that fail to develop mammary tumors (Siegel et al., page 559, 2nd col., 3rd parag.), while single transgenic mice did. As this relates to the instant invention, an artisan cannot predict what phenotype of a disease would result in cells expressing multiple transgenes and thus, an artisan is not enabled to use the claimed cells in any assay. Second, regarding the issue of cells comprising multiple gene disruptions, the art teaches that an artisan cannot predict what phenotypes would result from mice comprising two or more targeted disrupted genes of interest. The art teaches that the effects of gene disruption are not additive. For example, a disruption of biglycan and fibromodulin resulted in mice that exhibited a bone phenotype that was more severe than the phenotype exhibited by mice comprising a single disruption of the gene. These results indicated that the phenotype resulted from a synergistic effect of the two gene disruptions (Young et al., 2003, Glycoconjugate

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Journal, 19: 257-262, page 260, 2nd, col., 3rd parag.). As this applies to the instant invention, an artisan cannot predict that cells comprising multiple targeted gene disruptions would necessarily result in a cell with a predictable phenotype, wherein the cell has in vitro applications as a model for a disease. Third, in light of these issues of unpredictability of phenotype in making cells expressing a transgene or making cells comprising a disruption of a gene of interest, an artisan cannot reasonably predict how to make cells comprising a combination of disruptions and overexpression constructs, wherein the resulting cell is an in vitro model of disease. It should be pointed out that with regard to these cells comprising multiple chloride channel disruptions and/or multiple transgene constructs that express chloride channels, nothing in the specification or the art provide any guidance that certain combinations of gene disruptions and/or overexpression of chloride channels result in any human disease or disorder. It would be undue experimentation to make any kind of cell comprising gene disruptions and/or transgene overexpression constructs and correlate them with a specific human disease.

Because the claimed cells are not enabled, the method of using them to screen for substances are also not enabled.

The claimed invention encompasses cells that “do not express” or express only to a “reduced functional extent” (e.g. see claim 44) specific chloride channels. The Examiner had previously indicated that these terms encompass a wide breadth of mechanisms that could be used to achieve this state in the claimed cells and has also indicated that the art teaches that aspects of these mechanisms encompassed by the

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claims are unpredictable and not routine in the art (Office Action, May 19, 2005, pages 13-16). Applicant indicates on page 20, 3rd parag. of Applicant's response, December 20, 2005, that, "it is in our submission sufficient for an applicant to describe how a claimed invention can be made. There is in our submission no obligation on an applicant to describe how to succeed also using methods that may be more problematic and less desirable than those disclosed." In response, the issue at hand is that the claims broadly encompass a wide variety of methods in which "a reduced functional extent" of a chloride channel is achieved. In addition to a method of targeted gene disruption via homologous recombination could be used, the claim also encompasses methods such as antisense to reduce levels of mRNA transcript or use of a weakly expressing promoter to drive low amounts of a gene of interest. The art indicates that either of these methods is unpredictable (e.g. see Agrawal and Kanimalla reference and Goswami reference). While the specification teaches one aspect that is used to obtain cells that do not express a gene of interest (i.e. homologous recombination), this one aspect does not enable the full breadth of the genus of possible ways that this can be achieved. As such, the rejection regarding this issue is maintained.

For this reason, the specification and the art do not provide guidance for an artisan to arrive at the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-67 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims use the term, "functionally expressed." It is unclear what this term means. Does "functionally" refer to "expressed," which means that the invention being envisioned is an overexpression construct? Or, does "functionally" refer to the chloride channel? Nothing in the specification provide any guidance as to what this term is. Similarly, the claims use the term "preferentially functionally expressed." While the specification indicates that "preferentially" means "predominantly" (specification, page 5, 2nd parag.), it is unclear what is meant by "predominantly functionally expressed". Also, the claims use the phrase, "reduced functional extent". Does this phrase refer the levels of expression or to the activity of the chloride channels? The method claims depend on the claimed cells and are thus included in the rejection.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

